#19/Suppl Dec. 3/25

AM100012

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	:	Examiner: S. Chunduru
MARK ET AL.	)	
	:	Group Art Unit: 1656
Application No.: 09/425,501	)	
	:	
Filed: October 22, 1999	)	
	:	
For: PABLO, A POLYPEPTIDE THAT INTERACTS WITH BCL-XL, AND USES RELATED THERETO	)	
	:	March 1, 2002

The Assistant Commissioner for Patents
Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

I, Brad Ozenberger, declare the following in support of the above-identified application.

1. I hold a Ph.D. from the University of Missouri School of Medicine in with a major emphasis on Molecular Biology. I also hold a B.S. in Biology from the University of Missouri.

2. I currently serve as a Principal Research Scientist at Wyeth-Ayerst Research (a division of American Home Products Corporation) where I work on research and development in the Neurosciences Therapeutic Area. I have previously worked on

numerous gene discovery programs for multiple therapeutic indications.

3. I am a member of the American Association for the Advancement of Science and the Society for Neuroscience.

4. Because of my work, and my involvement in the Society for Neuroscience, I am very knowledgeable regarding the current literature, theory and recent developments relating to molecular neurosciences and apoptosis-related genes.

5. I am quite familiar with U.S. Patents, and I am named as inventor on eleven issued US patents and several patent applications. In performing my duties as a scientist, I have analyzed and scientifically evaluated numerous patents.

6. I am submitting this declaration on behalf of the assignee of the instant application in order to present proof of the novelty of the claimed invention relative to Nagase et al. (DNA Res., 3:321-329, 1996) hereinafter "Nagase" (Exhibit A).

7. I am familiar with the prosecution history of this patent application, having read in particular the specification, the present claims, and the Examiner's position regarding the prior art, as set forth in the Office Action dated June 28, 2001

(Exhibit B).

8. In order to compare the current invention to Nagase and in particular, to determine whether Nagase anticipates the current invention, I reviewed Nagase in light of my own knowledge of the state of the art relating to apoptosis and the molecular biology of neurons. Specifically, I reviewed Nagase in order to determine if that publication contains an enabling disclosure of the current invention.

9. The Examiner alleges that Nagase teaches the coding sequence of a cDNA clone from human myeloid cell line KG-1 and brain, wherein Nagase discloses a cDNA clone which is identical or [containing] absolute homology (100%) to the claimed sequences in SEQ ID Nos. 1 and 2 of the instant invention (see Exhibit B at page 4). The Examiner further alleges that Nagase discloses that the cDNA clones showed homology to genes that play key roles in regulation of developmental stages, apoptosis and cell-to-cell interaction.

10. As revealed by a careful reading of Nagase, the Examiner misstates the disclosure of Nagase.

11. The Nagase publication discloses a sequencing effort of human cDNA clones which attempted to identify as yet unidentified human genes. The effort managed to identify the sequences of 80 clones; and

the predicted coding sequences of the corresponding genes were designated KIAA0201 to KIAA0280.

10. The Examiner's assertion is based on the abstract which states:

> Computer search against the public databases indicated that ...58 genes carried sequences which show some similarities to known genes. Protein motifs that matched those in the PROSITE motif database were found in 25 genes and significant transmembrane domains were identified in 30 genes. Among the known genes to which significant similarity was shown, the genes that play key roles in regulation of developmental stages, apoptosis and cell-to-cell interaction were included. Abstract, emphasis added.

11. However, this is nothing more than a general statement, with no correlation between the 80 predicted coding sequences and functional, cellular activity of the encoded proteins. In fact, the cDNA clone designated KIAA0269, which is alleged to anticipate SEQ ID NO:1 of the invention, is suggested by Nagase to be most closely homologous (29.9%) to an extensin-like protein from *Zea mays* (see Exhibit A, Table 1). *Zea mays* is a species of corn. Tissue expression of KIAA0269 was observed in kidney, pancreas, thymus, testis, ovary, small intestine, colon, peripheral blood leukocytes and brain (Exhibit A, Table 3).

12. Table 2 of Nagase demonstrated that the

predicted sequence of KIAA0269 contained no known motifs or significant transmembrane domains.

13. Thus, there is nothing disclosed or described in Nagase suggesting that a protein encoded by the sequence of KIAA0269 would play a key role in regulation of developmental stages, apoptosis or cell-to-cell interaction. Indeed, Nagase did not reveal any use for the KIAA0269 sequence or a protein encoded by that sequence. Further, Nagase did not disclose how to use KIAA0269 or the protein encoded by that sequence.

14. Based on my knowledge of the state of the relevant art, no known method of using KIAA0269 or the protein encoded by that sequence existed prior to the present invention which discloses that the protein designated PABLO may be used to modulate BCL-XL in neurons.

15. Nagase merely discloses the primary structure of an unknown cDNA, but failed to enable any method of using the cDNA or the protein that sequence was predicted to encode.

16. These observations lead me to conclude that Nagase did not put the public in possession of the instant invention.

11. Further, Nagase failed to anticipate the present

invention because Nagase failed to provide an enabling disclosure.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application or any patent issuing thereon.

Brad Ozenberger

Brad Ozenberger, Ph.D.
Principal Research Scientist

NOTARY

State of New Jersey }
County of Middlesex } ss:

On the 1st day of March 2002, Brad Ozenberger personally appeared before me, known by me to be the same person described in and who executed the foregoing instrument, and acknowledged that he executed the same, of his own free will and for the purposes set forth.

Marilyn Winkler

MARILYN WINKLER
NOTARY PUBLIC OF NEW JERSEY
MY COMMISSION EXPIRES 1/25/2007

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/425,501	10/22/99	MARK R	GNN-005

HM12/0628

LAHIVE & COCKFIELD LLP
28 STATE STREET
BOSTON MA 02109

EXAMINER	
CHUNDURU, S	
ART UNIT	PAPER NUMBER
1656	10

DATE MAILED: 06/28/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

2 - Mail Copy

Office Action Summary

Application No.	Applicant(s)	
09/425,501	MARK ET AL.	
Examiner	**Art Unit**	
Suryaprabha Chunduru	1656	

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *6-13 and 16-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

DETAILED ACTION

1. Applicant's election of Group I without traverse is acknowledged. Claims 1-4, 14 and 15 in Group I were elected by the applicants and are considered in this action for examination.

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see at least page 31 line 15 and page 96, line 9). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 2 is rejected under 35U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The current claim is drawn to a genus (fragments) of Bcl-xL nucleic acid comprising a nucleic acid encoding 70% amino acid homology to SEQ ID NO: 2, a binding domain which hybridizes to a complement of SEQ ID NO.1 and a nucleic acid encoding binding domain. This large genus is represented in the specification by the named SEQ ID Nos. 1 and 2. Thus, applicant has expressed possession of only one species in a genus, which comprises hundreds of millions of different possibilities. The written description guidelines note regarding such genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the

necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) Here, no common elements or attributes of the sequences are disclosed in the sequences with 70% homology. With regard to the sequences, which have 70% homology, this is insufficient to demonstrate identity of Bcl-xL binding function where no structural information regarding where in the protein the binding function resides. The recitation of amino acids 419-559 or 429-559 in Bcl-xL binding domain in claim 2 do not specify the exact site for binding. Further no information is given regarding a methodology to determine such common elements or attributes. Further, there is no description of fragments.

With regard to the written description, all of these claims encompass nucleic acid sequences different from those disclosed in the specific SEQ ID Nos: 1 and 2 which include modifications by permitted by the 70% language for which no written description is provided in the specification.

> It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the amino acid sequence of the disclosed SEQ ID Nos are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception or written description of any amino acids modified by addition,

insertion, deletion, substitution or inversion with the disclosed SEQ ID Nos but retaining correlative function in the claimed product.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1-4 and 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Nagase et al. (DNA Res., 3: 321-329, 1996).

Nagase et al. teaches the coding sequence of cDNA clone from human myeloid cell line KG-1 and brain wherein Nagase et al. disclose a cDNA clone which is identical or absolute homology (100%) to the claimed sequences in SEQ ID Nos. 1 and 2 of the instant invention (see sequence alignment from GenEmbl. and Swissprot_39 databases). Nagase et al. also disclose that the cDNA clones showed homology to the genes that play key roles in regulation of developmental stages, apoptosis and cell-to-cell interaction (see page 321, abstract). Thus the disclosure of Nagase et al. meets the limitations in the instant claim 1.

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on 703-308-1152. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-308-0294 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
June 27, 2001

JEFFREY FREDMAN
PRIMARY EXAMINER

Notice of References Cited	Application/Control No. 09/425,501	Applicant(s)/Patent Under Reexamination MARK ET AL.	
	Examiner Suryaprabha Chunduru	Art Unit 1656	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification	
	A	US- -				
	B	US- -				
	C	US- -				
	D	US- -				
	E	US- -				
	F	US- -				
	G	US- -				
	H	US- -				
	I	US- -				
	J	US- -				
	K	US- -				
	L	US- -				
	M	US- -				

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification	
	N	- -					
	O	- -					
	P	- -					
	Q	- -					
	R	- -					
	S	- -					
	T	- -					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
*	U	Nagase T et al. Prediction of the coding sequences of unidentified human genes. VI. The coding sequences of 80 new genes deduced by analysis of cDNA clones from cell line KG-1 and brain. DNA Res., 3: 321-329, 1996.
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Attachment for PTO-948 (Rev. 03/01, or earlier)
6/18/01

The below text replaces the pre-printed text under the heading, "Information on How to Effect Drawing Changes," on the back of the PTO-948 (Rev. 03/01, or earlier) form.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the Notice of Allowability. Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson. **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a).

Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.